SUPPORT FOR THE AMENDMENTS

Claim 16 is amended to include the description of Claims 18 and 19.

Support for the amendment of Claim 17 is found in original Claims 20 and 21.

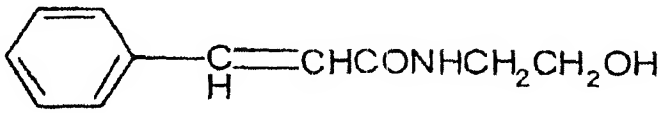
Claims 20 and 21 are amended to depend from Claim 17.

No new matter is believed added to this application by entry of this amendment.

Upon entry of this amendment, Claims 1-17 and 20-31 are active. Claims 1-15 are withdrawn.

REMARKS/ARGUMENTS

The claimed invention provides a method for treating rosacea by topical application of a dermatological composition containing idrocilamide. The chemical structure of idrocilamide is shown below:



The chemical name of idrocilamide is N-(2-hydroxyethyl)cinnamide. Applicants have described rosacea as follows (page 1, lines 8-15):

> Rosacea is a common, chronic and progressive inflammatory dermatitis associated with vascular instability. It mainly affects the central part of the face and is characterized by redness of the face or hot flushes, facial erythema, papules, pustules and telangiectasia. In serious cases, especially in men, the soft tissue of the nose may swell and produce a bulbous swelling known as rhinophyma.

Applicants have described that rosacea develops in four stages, beginning on page 2, line 8, of the specification, as follows:

> Rosacea develops in four stages, but passage through all the stages is not obligatory:

- stage 1 of vasomotor flushes (at about 20 years old). The patients have sudden bursts of paroxystic redness of the face and neck, with a hot sensation, but with no systemic signs. After the attacks, the skin of the face returns to normal. These "flushes" are triggered by changes in temperature (occasionally leading to thermophobia), and the intake of hot drinks or alcohol;

- stage 2 of erythemato-telangiectasia (at about 30 years old). The cheekbone areas are diffusely red. Dilated capillaries constituting standard acne rosacea are observed therein. In contrast with stage 1, the redness is permanent. Besides the cheeks, the chin and the middle of the forehead may be affected;

- stage 3 of papulo-pustules (at about 40 years old). Papules and pustules a few millimetres in diameter develop on a background of erythema, without associated comedones. This dermatitis may be very extensive, occasionally up to the bald part of the scalp in men, but is absent from the area around the mouth and the eyes. The patients complain of sensitive skin, with subjective intolerance to the majority of topical products and greasy cosmetics;

- stage 4 of rhinophyma (at about 50 years old or later). This late phase mainly affects men, in contrast with the other stages. The nose is increased in volume and diffusely red, and the follicular orifices are dilated. The skin gradually thickens.

Applicants respectfully note that Claim 16 is herein amended to recite that applying the composition comprises treating at least one of a first stage and a second stage of rosacea.

The rejection of Claims 16-31 under 35 U.S.C. 103(a) over Arkin et al. (WO 02/074290) in view of Barnwarth et al. (Tissue and systemic diffusion of idrocilamide after cutaneous administration) is respectfully traversed.

Arkin describes a topical preparation for treatment of rosacea which contains a non-steroidal anti-inflammatory drug classified according to chemical structure (page 4, lines 5-15) as follows:

- Salicylic acid derivatives (e.g., aspirin, sodium salicylate, choline magnesium trislicylate, diflunisal, salicylsalicyclic acid, sulfasalazine, olsalazine)
- Para-aminophenol derivatives (e.g., acetaminophen)
- Indole and indole acetic acids (e.g., indomethacin, sulindac, etodolac)
- Aryl acetic acids (e.g., tolmetin, diclofenac, ketorolac)
- Arylpropionic acids (e.g., ibuprofen, naproxen, flubiprofen,ketoprofen, fenoprofen, oxaprozin)

- Anthranilic acids (fenamates) (e.g. mefanamic acid, meclofenamic acid);
- Enolic acids (e.g., oxicams (piroxicam, tenoxicam), pyrazolidinediones (phenylbutazone, oxyphenthratazone)
- Alkanones (e.g., nabumetone).

Arkin does not expressly teach the inclusion of idrocilamide and Bannwarth to show this compound.

Bannwarth describes a study of the tissue and systemic distribution of idrocilamide in patients suffering from chronic arthropathy of the knee (page 2, lines 8-10; English translation).

Applicants submit that Arkin describes application of NSAID's to third stage rosacea as indicated in Clinical Trial 1 beginning on page 9 of the reference. Applicants note that results of the trial are gauged by a count of Papules and Pustules (See Tables 1 and 2) and as indicated in the above text from the specification, such dermal activity is associated with stage 3 of rosacea. Applicants submit that Arkin does not describe application to either one of stages 1 or 2 of rosacea.

In contrast, the present invention provides a method for treatment of rosacea, including treatment of at least one of stages 1 and 2.

In a discussion of "**Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.***" the Office has stated:

> The rationale to support a conclusion that the claim would have been obvious is that **all the claimed elements were known in the prior art** and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." **If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art, . . .** (Federal Register, Vol. 72, No. 195, page 57529) (Bold added) (Citations omitted)

Applicants respectfully submit that the cited combination of references does not describe or suggest a treatment for rosacea including at least one of the first two stages and therefore does not make all the elements of the presently claimed invention known. Therefore, according to the above KSR guidelines, a conclusion of obviousness cannot be supported and Applicants respectfully request that the rejection of Claims 16-31 under 35 U.S.C. 103(a) over Arkin in view of Barnwarth be withdrawn.

The rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph, is respectfully traversed.

Applicants note the M.P.E.P. § 2163 II. 2. states:

> Information which is well known in the art need not be described in detail in the specification. See e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)

The Office has pointed to the recitation of "cosmetic active agent," "skin calmative and protective agents" and "pro-penetrating agents" as failing to comply with the written description requirement. Applicants again respectfully submit that these terms are known in the art and that one of ordinary skill would recognize the meaning and substance of Applicants description.

Applicants respectfully note that the claimed invention is directed to a method for treating rosacea comprising applying topically to skin a pharmaceutical composition comprising idrocilamide. Rosacea as described above is associated with the facial skin tissue.

Therefore, known skin-care products such as described in the description of Skin-Care Products and Anti-acne Preparations in Kirk-Othmer Encyclopedia of Chemical Technology, Fifth Edition, Vol. 7, pp 842-844 (copy previously provided), would be recognized as cosmetic active agents according to the claimed invention.

Applicants pointed to page 6, lines 36-37, which state in pertinent part:

> . . .skin calmative and protective agents **such as allantoin** . . .

Applicants again submit that the description of allantoin as a skin calmative and protective agent conveys an understanding to one of ordinary skill in the art of the meaning of skin calmative and protective agent. A description of allantoin as a skin care product is attached. Applicants note that this material is an extract from the roots and leaves of the comfrey plant.

As further support for this term, Applicants provide attached a copy of page 686 from "Actifs et additifs en cosmetologie" which describes further examples of skin calmatives.

Applicants respectfully point to U.S. 7,316,810, Col. 4, lines 45-52, which describes propenetrating agents as follows:

> The propenetrating agent, which makes it possible to facilitate the penetration of the active principles, preferably dissolves the active principle present in the composition according to the invention. More particularly, it is chosen from volatile $C_1 - C_4$ alcohols, such as ethanol or isopropanol, from polyhydric alcohols, such as propylene glycol, and from glycol ethers such as ethoxydiglycol.

Finally, Applicants respectfully point to MPEP § 2163 II. 2. which provides the following guidance:

> The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the

> claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed.

Applicants submit that as described above, one of skill in the art would recognize the present claim elements to be implicit to the description of the specification and thus the present claim description is fully compliant with the written description requirement of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully request that the rejections of Claims 25 and 31 under 35 U.S.C. 112, first paragraph, be withdrawn.

The rejection of Claim 29 under 35 U.S.C. 112, first paragraph, is respectfully traversed.

An immunosuppressive agent is a medication that slows or halts immune system activity. Immunosuppressive agents may be given to prevent the body from mounting an immune response after an organ transplant or for treating a disease that is caused by an overactive immune system.

Applicants have previously submitted a listing of known immunosuppressive agents (encyclopedia of medical concepts) and respectfully submit that such clear definition clearly complies with the written description requirement.

Applicants again submit that anti-proliferative agents are related to « Chemotherapy " which is treatment of cancer with anticancer drugs. Chemotherapy drugs are classified based on how they work. The main types of chemotherapy drugs are described below:

· Alkylating drugs kill cancer cells by directly attacking DNA, the genetic material of the genes. Cyclophosphamide is an alkylating drug.

· Antimetabolites interfere with the production of DNA and keep cells from growing and multiplying. An example of an antimetabolite is 5-fluorouracil (5-FU).

· Antitumor antibiotics are made from natural substances such as fungi in the soil. They interfere with important cell functions, including production of DNA and cell proteins. Doxorubicin and bleomycin belong to this group of chemotherapy drugs.

· Plant alkaloids prevent cells from dividing normally. Vinblastine and vincristine are plant alkaloids obtained from the periwinkle plant.

· Steroid hormones slow the growth of some cancers that depend on hormones. For example, tamoxifen is used to treat breast cancers that depend on the hormone estrogen for growth.

Applicants again respectfully submit that in view of the above, Claim 29 does comply with the written description requirement. Accordingly, Applicants respectfully request that the rejections of Claim29 under 35 U.S.C. 112, first paragraph, be withdrawn.

Applicants respectfully submit that the above-identified application is now in condition for allowance and early notice of such action is earnestly solicited.

Respectfully submitted,

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